



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/668,665

09/23/2003

Jean-Claude Yvin

16721-0240
(42528-292744)

1061

881 7590 11/14/2006

STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

EXAMINER

ISSAC, ROY P

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/668,665

Applicant(s)

YVIN ET AL.

Examiner

Roy P. Issac

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 11 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 4-10 is/are pending in the application.
- 4a) Of the above claim(s) 11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1 and 4-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is in response to Applicant's response (remarks/Argument/ Amendment to the claims) filed 11 October 2006, wherein claims 1, 4-6 and 10 were amended, and claims 2-3 were cancelled. Claim 11 was withdrawn from consideration as being drawn to a non-elected invention. Any objection or rejection not expressly repeated has been withdrawn.

Rejections Withdrawn

Claims 1, 4-7 and 10 were rejected on the grounds of non-statutory obviousness-type double patenting over the claims of U.S. Patent No.6,750,208, in view of Kim et. al. Since the applicants have submitted a terminal disclaimer of the prior U.S. Patent No. 6,750,208 the rejection is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5-7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yvin et. al. (WO 99/39718) in view of Kim et. al. (Carbohydr. Res. 2000).

The examiner has reconsidered the overall teaching of Yvin. As discussed previously, Yvin teaches the method of treating disorders resulting from apoptosis dysfunction comprising the administration of β -glucan oligosaccharides. The reference describes cancer as one such disorder. See reference claim 8 and the paragraph bridging pages 3 and 4. The activities recited in claims 5 and 6 are inherent activities that would result from the administration of the oligosaccharide whether or not it was recognized in the original reference. The reference describes the oligosaccharides contemplated as branched or linear (1,3)- β -glucans having 3 to 150 monosaccharides in the backbone. See Formula I at page 5. The reference further suggests the use of oligosaccharides resulting from depolymerization of laminarian. See reference claim 5. The reference does not exemplify the use of the oligosaccharides recited in the instant claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to select any of the oligosaccharides described by Yvin to administer for their art-disclosed utility of the treatment of cancer. The artisan would have been motivated to select oligosaccharides in the size range of the instant method because they are commercially available and soluble for ease of administration to the patient. See Kim at Table 1 and first paragraph in section 2. One of ordinary skill in the art would have reasonable expectation of success in using these lower oligosaccharides for the treatment of cancer because Yvin had disclosed this utility. There may be some unexpected results in the use of the recited oligosaccharides, but none has been demonstrated. It would be within

Art Unit: 1623

the scope of the practitioner to select an appropriate method of administration through routine experimentation.

Response to Arguments

Applicant's arguments filed 11 October, 2006 with respect to this rejection of claims 1, 5-7 and 10 made under 35 U.S.C. §103(a) over Yvin et. al. (WO 99/39718) in view of Kim et. al. of record in the previous Office Action have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

Applicants assert that the laminaritetraose and laminaripentaose unexpectedly exhibit significantly higher anti-cancer activity than laminarin. Applicants use example 7, (results, table 6) to support their argument. The results from example 7, reported in table 6 is shown in its entirety below. (Page 28)

Table 6

	<u>24 hours</u>	<u>48 hours</u>
Laminaritetraose	28.1	35.9
Laminaripentaose	79.6	38.7
Laminarin	19.4	-

This study compares one data point for the two compounds of the instant application with laminarin. Laminaritetraose cannot be said to have a significantly higher activity than laminarin. The comparison for the only other reported data point for laminarin is missing. Furthermore, the activity of laminaripentaose has significantly decreased in the 48 hour data.

Art Unit: 1623

Applicant's attention is drawn to a more comprehensive study reported in the instant application. Table 5 reports the results of comparison of laminaripentaose and laminaritetraose with lentinan. The results are as follows. (Page 27).

Table 5 :Concentration of TNF alpha in pg/ml of blood of treated mice after different durations of treatment

	30 min	60 min	90 min
Laminaritetraose 50µm/mouse	55.7	103.0	35.3
Laminaripentaose 50µm/mouse	34.3	37.0	71.3
Lentinan 50µm/mouse	20	15.7	32.0
Laminaritetraose 100µm/mouse	39.0	18.4	13.6
Laminaripentaose 100µm/mouse	53.0	46.5	93.2
Lentinan 100µm/mouse	28	30.7	20.3
Laminaritetraose 250µm/mouse	27.3	152.3	11.1
Laminaripentaose 250µm/mouse	42.1	36.4	24.4
Lentinan 250µm/mouse	86.3	68.7	48.6

This comparison shows that lentinan's activity is better than that of laminaripentaose at 250µM concentration at all time points. The data from laminaritetraose is inconsistent at the 250µM level because it goes from 27.3 to 152.3 and then comes back to 11.1 in 30, 60 and 90 minute time intervals. It is not clear which of these data points is the reliable indicator of the activity of these compounds.

Furthermore, as the applicants pointed out in their response filed 11 October 2006, Yvin et. al. discloses β -(1,3)-glucan having preferably 15-30

Art Unit: 1623

glucose units. (Page 6, Paragraph 3). One of ordinary skill in the art will consider β -(1,3)-glucans having 15-30 glucose units as closer prior art than lentinan or laminarin both of which contains a mixture of polymers with varying lengths. As such, the applicants have not compared the unexpected results to the closest prior art. To establish unexpected results over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range. *In re Hill*, 284 F.2d 955, 128 USPQ 197 (CCPA 1960). The applicants have made no such comparisons here. (MPEP 716.02).

As noted in MPEP (716.02), any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, one of ordinary skill in the art will view that a difference that is to the extent that is really is unexpected is absent.

Applicants further argue that Yvin et. al. fails to teach specific oligo- β -glucans of claim 1. As discussed previously, Yvin teaches the method of treating disorders resulting from apoptosis dysfunction comprising the administration of β -glucan oligosaccharides. Even though the specific oligo- β -(1,3)-glucan polymers of 3-9 units are not disclosed, Yvin et. al. disclosed polymers of 3-150 monosaccharides. Furthermore, Kim et. al. discloses the particular compounds of the instant invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking

Art Unit: 1623

references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

As discussed above, one of ordinary skill in the art would have been motivated to select oligosaccharides in the size range of the instant method because they are commercially available and soluble for ease of administration to the patient. For the above stated reasons, said claims are properly rejected under 35 U.S.C § 103(a). Therefore, said rejection is adhered to.

Rejection over Yvin et. al. in view of Kim et.al. further in view of Hillman et. al.

Claims 1, 4-7 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yvin et. al. (WO 99/39718) in view of Kim et. al. (Carbohydr. Res. 2000), further in view of Hillman et. al. (U.S. Patent No. 5,858,715).

The disclosure of Yvin et. al. and Kim et. al. discussed above.

Hillman et. al. teaches the treatment of diseases comprising impaired apoptosis. These include a variety of cancers, such as lung, breast, ovarian, and colon. See abstract and Col. 16, lines 45-53.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the recited oligosaccharides to treat cancers taught by Hillman to comprise decreased apoptosis. One of ordinary skill would reasonably expect success in such treatment because Yvin had taught that the oligosaccharides have utility in such treatment. It would further be within the

Art Unit: 1623

scope of the artisan to select any appropriate method of administration with routine experimentation.

Response to Arguments

Applicant's arguments filed 11 October, 2006 with respect to this rejection of claims 1, 4-7 and 10 made under 35 U.S.C. § 103(a) over Yvin et. al. (WO 99/39718) in view of Kim et. al. of record in the previous Office Action have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

The applicants argue that one of ordinary skill in the art would have never incited to expect that laminaritetraose and laminaipentaose have significantly higher anti cancer activity than long-chain glucans such as laminarin.

Applicants arguments concerning Yvin et.al. and Kim et. al. as well as the alleged unexpected results are discussed above.

As discussed above, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the recited oligosaccharides to treat cancers taught by Hillman to comprise decreased apoptosis. One of ordinary skill would reasonably expect success in such treatment because Yvin had taught that the oligosaccharides have utility in such treatment. It would further be within the scope of the artisan to select any appropriate method of administration with routine experimentation. For the above stated reasons, said claims are properly rejected under 35 U.S.C § 103(a). Therefore, said rejection is adhered to.

Art Unit: 1623

Rejection over Yvin et. al. in view of Kim et.al. further in view of Penney et. al.

Claims 1 and 5-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yvin et. al. (WO 99/39718) in view of Kim et. al. (Carbohydr. Res. 2000), further in view of Penney et. al. (U.S. Patent No. 5,688,771).

The disclosure of Yvin et. al. and Kim et. al. discussed above.

Penney teaches the use of immunomodulatory peptides, alone, or in combination with chemotherapeutic agents for the treatment of cancer.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to administer the oligosaccharides taught by Yvin in combination with an immunomodulatory agent/and or chemotherapeutic agent. Given that all these agents are known to have utility for the treatment of cancer, one of ordinary skill in the art would be motivated to administer them in combination for their combined effects. It would further be within the scope of the artisan to select any appropriate method of administration with routine experimentation.

Response to Arguments

Applicant's arguments filed 11 October, 2006 with respect to this rejection of claims 1 and 5-10 made under 35 U.S.C. §103(a) over Yvin et. al. (WO 99/39718) in view of Kim et. al, further in view of Penney et. al. of record in the previous Office Action have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

Art Unit: 1623

The applicants argue that one of ordinary skill in the art would have never incited to expect that laminaritetraose and laminaipentaose have significantly higher anti cancer activity than long-chain glucans such as laminarin.

Applicants arguments concerning Yvin et.al. and Kim et. al. as well as the alleged unexpected results are discussed above.

As dicussed above, it would have been obvious to one having ordinary skill in the art at the time the invention was made to administer the oligosaccharides taught by Yvin in combination with an immunomodulatory agent/and or chemotherapeutic agent. Given that all these agents are known to have utility for the treatment of cancer, one of ordinary skill in the art would be motivated to administer them in combination for their combined effects. For the above stated reasons, said claims are properly rejected under 35 U.S.C § 103(a). Therefore, said rejection is adhered to.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

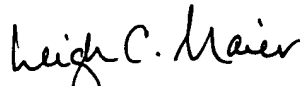
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1623

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Roy P. Issac
Patent Examiner
Art Unit 1623
03 November 2006


Leigh C. Maier
Primary Examiner
Art Unit 1623